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10/769,574	01/29/2004	Bret Berner	66631.8001.US01	8962

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King & Spalding LLP
P.O. Box 889
Belmont, CA 94002-0889

EXAMINER	
HOLT, ANDRIAE M	
ART UNIT	PAPER NUMBER
1616	
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Please find below and/or attached an Office communication concerning this application or proceeding.

The time period for reply, if any, is set in the attached communication.

Office Action Summary	Application No.	Applicant(s)	
	10/769,574	BERNER ET AL.	
	Examiner	Art Unit	
	Andriae M. Holt	1616	

-- The MAILING DATE of this communication appears on the cover sheet with the correspondence address --

Period for Reply

A SHORTENED STATUTORY PERIOD FOR REPLY IS SET TO EXPIRE *3* MONTH(S) OR THIRTY (30) DAYS, WHICHEVER IS LONGER, FROM THE MAILING DATE OF THIS COMMUNICATION.

- Extensions of time may be available under the provisions of 37 CFR 1.136(a). In no event, however, may a reply be timely filed after SIX (6) MONTHS from the mailing date of this communication.
- If NO period for reply is specified above, the maximum statutory period will apply and will expire SIX (6) MONTHS from the mailing date of this communication.
- Failure to reply within the set or extended period for reply will, by statute, cause the application to become ABANDONED (35 U.S.C. § 133). Any reply received by the Office later than three months after the mailing date of this communication, even if timely filed, may reduce any earned patent term adjustment. See 37 CFR 1.704(b).

Status

1)☒ Responsive to communication(s) filed on *22 April 2010*.

2a)☒ This action is **FINAL**. 2b)☐ This action is non-final.

3)☐ Since this application is in condition for allowance except for formal matters, prosecution as to the merits is closed in accordance with the practice under *Ex parte Quayle*, 1935 C.D. 11, 453 O.G. 213.

Disposition of Claims

4)☒ Claim(s) *1,5,8-20 and 22-31* is/are pending in the application.

4a) Of the above claim(s) *15-17 and 29* is/are withdrawn from consideration.

5)☐ Claim(s) _____ is/are allowed.

6)☒ Claim(s) *1,5,8-14,18-20,22-28,30 and 31* is/are rejected.

7)☐ Claim(s) _____ is/are objected to.

8)☐ Claim(s) _____ are subject to restriction and/or election requirement.

Application Papers

9)☐ The specification is objected to by the Examiner.

10)☐ The drawing(s) filed on _____ is/are: a)☐ accepted or b)☐ objected to by the Examiner.

Applicant may not request that any objection to the drawing(s) be held in abeyance. See 37 CFR 1.85(a).

Replacement drawing sheet(s) including the correction is required if the drawing(s) is objected to. See 37 CFR 1.121(d).

11)☐ The oath or declaration is objected to by the Examiner. Note the attached Office Action or form PTO-152.

Priority under 35 U.S.C. § 119

12)☐ Acknowledgment is made of a claim for foreign priority under 35 U.S.C. § 119(a)-(d) or (f).

a)☐ All b)☐ Some * c)☐ None of:

1.☐ Certified copies of the priority documents have been received.

2.☐ Certified copies of the priority documents have been received in Application No. _____.

3.☐ Copies of the certified copies of the priority documents have been received in this National Stage application from the International Bureau (PCT Rule 17.2(a)).

* See the attached detailed Office action for a list of the certified copies not received.

Attachment(s)

1) ☒ Notice of References Cited (PTO-892)
2) ☐ Notice of Draftsperson's Patent Drawing Review (PTO-948)
3) ☒ Information Disclosure Statement(s) (PTO/SB/08) Paper No(s)/Mail Date *4/22/2010*.
4) ☐ Interview Summary (PTO-413) Paper No(s)/Mail Date. _____ .
5) ☐ Notice of Informal Patent Application
6) ☐ Other: _____.

DETAILED ACTION

This Office Action is in response to Applicant's amendment filed April 22, 2010. Claims 1, 5, 8-20, and 22-31 are pending in the application. Claims 1 and 5 have been amended. Claims 30-31 are newly added. Claims 15-17and 29 remain withdrawn from consideration as being drawn to a nonelected species in the previous office action. Claims 1, 5, 8-14, 18-20, 22-28, and 30-31 will presently be examined to the extent they read on the elected subject matter of record.

Upon further review and search update of the art provided on the IDS submitted on 4/22/2010, claims 5, 8-10, and 22-28, which were previously objected to as being dependent upon a rejected base claim, but would be allowable if rewritten in independent form including all of the limitations of the base claim and any intervening claims, will be included in the Double Patenting rejection. It is noted that the therapeutically effective amount of the active agent of claims 8-10 is related to the weight ratio of drug to polymer in the solid polymeric matrix of claim 19 of US Patent Application 6,340,475. As such, the therapeutically effective amount is dependent on the polymer present in each application, especially when the weight ratio of the drug to polymer is from about 0.01:99.99 to about 80:20, which means the active agent will be present in an amount of 0.01% to 80% and as each is drawn to a method of delivering a pharmacologically active agent from a table dosage form comprised of a polymer matrix and a pharmacologically active agent dispersed in the matrix. Therefore, the indication of allowability of claims 5, 8-10, and 22-28 if rewritten in independent form **is withdrawn**.

Status of the Claims

Rejections and/or objections not reiterated from the previous Office Action are hereby withdrawn. The following rejections and/or objections are newly applied. They constitute the complete set of rejections presently being applied to the instant application.

Double Patenting

The nonstatutory double patenting rejection is based on a judicially created doctrine grounded in public policy (a policy reflected in the statute) so as to prevent the unjustified or improper timewise extension of the "right to exclude" granted by a patent and to prevent possible harassment by multiple assignees. A nonstatutory obviousness-type double patenting rejection is appropriate where the conflicting claims are not identical, but at least one examined application claim is not patentably distinct from the reference claim(s) because the examined application claim is either anticipated by, or would have been obvious over, the reference claim(s). See, e.g., *In re Berg*, 140 F.3d 1428, 46 USPQ2d 1226 (Fed. Cir. 1998); *In re Goodman*, 11 F.3d 1046, 29 USPQ2d 2010 (Fed. Cir. 1993); *In re Longi*, 759 F.2d 887, 225 USPQ 645 (Fed. Cir. 1985); *In re Van Ornum*, 686 F.2d 937, 214 USPQ 761 (CCPA 1982); *In re Vogel*, 422 F.2d 438, 164 USPQ 619 (CCPA 1970); and In *re Thorington*, 418 F.2d 528, 163 USPQ 644 (CCPA 1969).

A timely filed terminal disclaimer in compliance with 37 CFR 1.321(c) or 1.321(d) may be used to overcome an actual or provisional rejection based on a nonstatutory double patenting ground provided the conflicting application or patent either is shown to be commonly owned with this application, or claims an invention made as a result of activities undertaken within the scope of a joint research agreement.

Effective January 1, 1994, a registered attorney or agent of record may sign a terminal disclaimer. A terminal disclaimer signed by the assignee must fully comply with 37 CFR 3.73(b).

Claims 1, 8-14, and 30-31 are rejected on the ground of nonstatutory obviousness-type double patenting as being unpatentable over claims 19-20 and 40 of U.S. Patent No. 6,340,475. Although the conflicting claims are not identical, they are not patentably distinct from each other because both applications are directed towards a method of delivering a pharmacologically active agent by orally administering to a

patient in the fed mode a therapeutically effective amount of the active agent and at least one biocompatible, hydrophilic polymer that swells upon absorption of water from gastric fluid in order to promote gastric retention. In the instant claims, the dosage form is a matrix/active agent tablet, wherein the active is ciprofloxacin. Claim 19 in U.S. Patent No. 6,340,475 does not provide for a matrix/active agent tablet dosage, however, it does provide a solid polymeric matrix wherein the drug is dispersed therein at a weight ratio of drug to polymer of from about 0.01:99.9 to about 80:20. Therefore, it would have been obvious to the skilled artisan that the dosage form could be a matrix/active tablet dosage. It would have been obvious to one skilled in the art that the drug would have been dispersed in a polymeric matrix that is water-swellable rather than merely hydrophilic and that has an erosion rate that is substantially slower than its swelling rate, and that releases the drug primarily by diffusion, as taught in the specification. It would have been obvious to the skilled artisan that the therapeutically effective amount of drug present in the formulation is dependent on the polymer present in each application, especially when the weight ratio of the drug to polymer is from about 0.01:99.99 to about 80:20, Patent No. 6,340,475, and as each is drawn to a method of delivering a pharmacologically active agent from a tablet dosage form comprised of a polymer matrix and a pharmacologically active agent dispersed in the matrix. The active agent that is being administered is the same active agent, especially wherein the therapeutically effective amount of the active amount is the same 0.01% to 80%,claims 8-10 of the instant application and claims 19 and 40 of US Patent No. 6.340,475. As the amount of active agent present is the same in each and each are

dispersed in the same polymer matrix, the properties of each of the formulations are the same. Therefore, the scopes of the copending claims overlap and thus they are obvious variants of one another.

Response to Arguments

Applicant's arguments filed April 20, 2010 have been fully considered but they are not persuasive. Applicant argues that by amending independent claim 1 to add the limitations of claim 4, "wherein at least 75 wt % of the active agent in the dosage form is released within the time period" places the claim in condition for allowance. In response to Applicant's arguments, the amendment to the claims continues to be an obvious variant of the claims in U.S. Patent No. 6,340,475. Applicant's claims are specifically directed to the administration of an active agent dispersed in a polymer matrix. The active agents of the instant application and US Patent No. 6.340,475 are the same. They have the same amount of active agent, 0.01% to 80%, and are each dispersed in a polymer matrix, which would inherently have the same amount of polymer present in the matrices. Each when administered a) upon imbibition of water swells unrestrained dimensionally to a size effective to promote gastric retention and b) maintains its size for an extended period of time before it diminishes by erosion. The release of the active agent from the dosage form is based the amount of active and polymer present in the formulations. As, these are the same, the release time period would be an inherent property of the formulations, the formulations will behave in the same manner. Applicant should distinguish how the end formulations, the matrix/active agent tablet of instant

application and solid polymeric matrix that contains drug of U.S. Patent No. 6,340,475, differ to overcome the Double Patenting rejection or file a terminal disclaimer.

New Rejection Necessitated by the IDS submission on April 22, 2010

Claim Rejections - 35 USC § 103

The following is a quotation of 35 U.S.C. 103(a) which forms the basis for all obviousness rejections set forth in this Office action:

> (a) A patent may not be obtained though the invention is not identically disclosed or described as set forth in section 102 of this title, if the differences between the subject matter sought to be patented and the prior art are such that the subject matter as a whole would have been obvious at the time the invention was made to a person having ordinary skill in the art to which said subject matter pertains. Patentability shall not be negatived by the manner in which the invention was made.

This application currently names joint inventors. In considering patentability of the claims under 35 U.S.C. 103(a), the examiner presumes that the subject matter of the various claims was commonly owned at the time any inventions covered therein were made absent any evidence to the contrary. Applicant is advised of the obligation under 37 CFR 1.56 to point out the inventor and invention dates of each claim that was not commonly owned at the time a later invention was made in order for the examiner to consider the applicability of 35 U.S.C. 103(c) and potential 35 U.S.C. 102(e), (f) or (g) prior art under 35 U.S.C. 103(a).

Claims 1, 5, 8-14, 18-20, 22-28, and 30-31 are rejected under 35 U.S.C. 103 (a) as being unpatentable over Penners et al. (CA 2,143,500) in view of the Ciprofloxacin Patient Information Sheet and the Cipro® Drug Information Sheet (2000).

Applicant's Invention

Applicant claims a method of delivering a pharmacologically active agent, ciprofloxacin, orally to a patient in a fed mode. Applicant claims the method comprising

combining the ciprofloxacin with at least one biocompatible, hydrophilic polymer which upon imbibition of water swells unrestrained dimensionally to a size effective to promote gastric retention and maintains its size for an extended period of time before it is diminished by erosion. Applicant also claims a method for treating a human patient suffering from a bacterial infection that is responsive to the oral administration of ciprofloxacin, comprising orally administering to the subject in a fed mode a therapeutically effective amount of the dosage form.

Determination of the scope of the content of the prior art (MPEP 2141.01)

Penners et al. teach an administration form having a prolonged gastric residence time, comprising: (I) an acid insensitive active compound or a combination and (II) a gel-forming agent comprising a homogenous mixture of polymers (III) containing lactam groups and polymers (IV) containing carboxyl groups which is distinguished in acidic aqueous media by marked swelling properties. Penners et al. teach by "marked swelling properties" is meant that the volume of the administration form, e.g., the tablet, is increased about five-fold or more (page 7, lines 24-30-page 8, lines 1-9). Penners et al. teach the administration of an individual dose of a medicament form which the active compound is released in a controlled manner over a prolonged period has the advantage that over a prolonged period a constant and uniform blood level of the active compound is guaranteed (page 1, lines 15-20). Penners et al. teach suitable active compounds are those which are suitable for oral administration and for sustained-released therapy (page 10, lines 18-21). Penners et al. teach the administration forms

are particularly suitable for active compounds which display their absorption window in the stomach or in the upper part of the gastrointestinal tract, such as ciprofloxacin (page 10, lines 22-28). Penners et al. teach the amount of active compound contained in the administration forms can be different, depending on the nature of the active compound, the degree of delay of release of the active compound desired and the type of construction of the administration form (page 11, lines 25-27-page 12, lines1-2). Penners et al. teach the tablet embodiment of the administration form is particularly advantageous. The active compound can be compressed together with the polymers and optionally other auxiliaries customary in pharmaceutical technology to give a homogeneous tablet (page 12, lines 3-10). Penners et al. teach the swelling properties of the administration forms, and also their mechanical stability in the swollen state, is affected substantially by the mixing ratio of the two polymers. Penners et al. teach that the intense mixing of the polymers essentially determines the good swelling properties and the mechanical stability of the administration forms prepared (page 9a, lines 1-14). Penners et al. teach that it is common in all embodiments that they swell strongly in the stomach, and as a result, reside in the stomach for a relatively long time (page 13, lines 15-17). Penners et al. teach in example 5 the preparation of a monolayer tablet. The substances used are ciprofloxacin-HCl- 250 mg/tablet (50% of the tablet), gel mixture, Luviskol K 90:Eudragit L, which is the polymer matrix-229.8 mg/tablet, and sodium bicarbonate powder-20.2 mg/tablet. The release of the active compound from the tablets was determined in a customary release apparatus. In the course of 24 hours the tablets released the active compound completely. During the course of this they

absorbed so much liquid that their diameter was 3 cm with good mechanical stability (page 17, lines 1-20-page 18, lines 1-15).

Ascertainment of the difference between the prior art and the claims (MPEP 2141.02)

Penners et al. do not explicitly disclose the medication is administered to a patient in a fed mode, that it is diminished by erosion after it maintains its size for an extended period of time, or that is it used for treating a human patient suffering from a bacterial infection that is responsive to the oral administration of ciprofloxacin, comprising orally administering to the subject in a fed mode a therapeutically effective amount of the dosage form. It is for this reason the Ciprofloxacin Patient Information Sheet and the Cipro Drug Information Sheet are added as secondary references.

The Ciprofloxacin Patient Information Sheet teaches that ciprofloxacin may be taken with or without food. It is preferable to take ciprofloxacin 2 hours after a meal (fed mode).

The Cipro ® (ciprofloxacin hydrochloride) Tablets and Cipro® (ciprofloxacin) Drug Information Sheet teach that Cipro® is a synthetic broad spectrum antimicrobial agent for oral administration (page 1, Description). The Drug Information Sheet teaches on pages 5-6 that Cipro® is shown to be active against Pseudomonas, Shigella, Salmonella, E. coli, Campylobacter, Enterobacter and *Bacillus anthracis.*

Finding of prima facie obviousness
Rationale and Motivation (MPEP 2142-2143)

It would have been obvious to one of ordinary skill in the art at the time of invention to combine the teachings of Penners et al., the Cipro Patient Information Sheet, and the Cipro Drug Information Sheet and administer the medication in a fed mode. One skilled in the art at the time the invention was made would have been motivated to administer the formulation in a fed mode because the Cipro Patient Information Sheet indicates that ciprofloxacin is preferably taken 2 hours after a meal, in which time the subject would be in the fed mode.

It would have been obvious to one of ordinary skill in the art at the time of invention to combine the teachings of Penners et al., the Cipro Patient Information Sheet, and the Cipro Drug Information Sheet and know that the tablet dosage is diminished by erosion after it maintains its size for an extended period of time. One skilled in the art at the time the invention was made would know that the tablet dosage is diminished by erosion after it maintains its size for an extended period of time because Penners et al. teach that in all embodiments of the formulations they swell strongly in the stomach, and as a result, reside in the stomach for a relatively long time, based on the nature of the polymers used to form the matrix. It would have been obvious to the skilled artisan that as the active agent is released from the polymers, the polymers will erode over a period time because of the nature of the polymers and acidic environment of the gastrointestinal system.

It would have been obvious to one of ordinary skill in the art at the time of invention to combine the teachings of Penners et al., the Cipro Patient Information Sheet, and the Cipro Drug Information Sheet and use the formulations to treat a human

patient suffering from a bacterial infection that is responsive to the oral administration of ciprofloxacin, comprising orally administering to the subject in a fed mode a therapeutically effective amount of the dosage form. One skilled in the art at the time the invention was made would have been motivated to use the formulations to treat a human patient suffering from a bacterial infection because the Cipro ® Drug Information Sheet teaches that Cipro® is a synthetic broad spectrum antimicrobial agent for oral administration. In addition, the Drug Information Sheet teaches on that Cipro® is shown to be active against Pseudomonas, Shigella, Salmonella, E. coli, Campylobacter, Enterobacter and *Bacillus anthracis,* known bacteria that cause bacterial infections.

Each reference is silent to the dosage form being characterized by an erosion rate to dissolution rate of approximately 1.1:1 to 5:1. It would have been obvious to the skilled artisan that the erosion ratio to dissolution rate would be dependent on the make-up of the polymer drug matrix and these properties would be inherent properties of the polymers and active ingredients used in the formulations and the amounts of each component used in the formulations. Therefore, since Penners et al. teach administration forms having a prolonged gastric residence time, comprising: (I) an acid insensitive active compound or a combination and (II) a gel-forming agent comprising a homogenous mixture of polymers (III) containing lactam groups and polymers (IV) containing carboxyl groups which is distinguished in acidic aqueous media by marked swelling properties, these formulations would inherently have erosion rates and dissolution rates that will characterize the drug formulations.

Conclusion

Applicant's submission of an information disclosure statement under 37 CFR 1.97(c) with the fee set forth in 37 CFR 1.17(p) on April 22, 2010 prompted the new ground(s) of rejection presented in this Office action. Accordingly, **THIS ACTION IS MADE FINAL**. See MPEP § 609.04(b). Applicant is reminded of the extension of time policy as set forth in 37 CFR 1.136(a).

A shortened statutory period for reply to this final action is set to expire THREE MONTHS from the mailing date of this action. In the event a first reply is filed within TWO MONTHS of the mailing date of this final action and the advisory action is not mailed until after the end of the THREE-MONTH shortened statutory period, then the shortened statutory period will expire on the date the advisory action is mailed, and any extension fee pursuant to 37 CFR 1.136(a) will be calculated from the mailing date of the advisory action. In no event, however, will the statutory period for reply expire later than SIX MONTHS from the mailing date of this final action.

Information regarding the status of an application may be obtained from the Patent Application Information Retrieval (PAIR) system. Status information for published applications may be obtained from either Private PAIR or Public PAIR. Status information for unpublished applications is available through Private PAIR only. For more information about the PAIR system, see http://pair-direct.uspto.gov. Should you have questions on access to the Private PAIR system, contact the Electronic Business Center (EBC) at 866-217-9197 (toll-free). If you would like assistance from a USPTO Customer Service Representative or access to the automated information system, call 800-786-9199 (IN USA OR CANADA) or 571-272-1000.

Any inquiry concerning this communication or earlier communications from the examiner should be directed to Andriae M. Holt whose telephone number is 571-272-9328. The examiner can normally be reached on 9:00 am-5:00 pm.

If attempts to reach the examiner by telephone are unsuccessful, the examiner's supervisor, Johann Richter can be reached on 571-272-0646. The fax phone number for the organization where this application or proceeding is assigned is 571-273-8300.

Andriae M. Holt
Patent Examiner
Art Unit 1616

/Johann R. Richter/

Supervisory Patent Examiner, Art Unit 1616